

### REMARKS

After entry of this amendment, claims 1-22 and 24-31 are pending, of which claims 6-22, 24-26 and 29-30 are withdrawn. Applicants respectfully request entry of the above claim amendments as they are believed to put the claims in condition for allowance or, alternatively, in better form for consideration on appeal. Thus, entry under 37 C.F.R. 1.116 is correct. Claim 23 has been cancelled without prejudice or disclaimer. Withdrawn claim 24 has been amended to correct the dependency due to the cancellation of claim 23. New claim 31 has been added and finds support *inter alia* in Figures 3-7. The new claim further narrows down the scope of the independent claim and thus, does not present any new issues that require further consideration or search. Additionally, the total number of claims is not increased in view of the cancellation of claim 23. No new matter has been added.

In the event that the elected product claims are found allowable, Applicants respectfully request rejoinder of the linked inventions, claims drawn to methods of using the product, and claims which depend from or otherwise include all the limitations of the allowed product claim. MPEP § 821.04(b).

Claims 1-4 and 27-28 remain rejected under 35 U.S.C. § 103(a) as being obvious over Dujon *et al.* (hereinafter "Dujon"). Applicants respectfully disagree and traverse the rejection for the reasons of record and for the following additional reasons.

The Examiner relies on Dujon for teaching a recombination system comprising a vector having, in the 5' to 3' direction, a LTR sequence, a I-SceI recognition site, a selection marker, another copy of the LTR sequence, I-SceI recognition site and a second selection marker as illustrated in Figure 25 of Dujon. Office Action dated December 26, 2007. The Examiner acknowledges that Dujon does not teach that the disclosed transgenic sequence does not contain any I-SceI recognition site as required by the claims, but alleges that it would have been obvious to one skilled in the art to modify the vector of Dujon by deleting one of the I-SceI sites contained in the disclosed constructs. The Examiner contends that one of ordinary skill in the art would have been motivated to do so given the teaching of Dujon that either one of the I-SceI sites alone is sufficient to produce the same recombinant transgenic sequence. Additionally, the Examiner asserts that, because it would have been obvious to one skilled artisan to delete the right I-SceI site, the only remaining I-SceI site is located between two homologous sequences.

Applicants respectfully disagree on the basis that the prior art does not suggest or motivate the proposed modification.

As an initial matter, it is noted that “a claim preamble has the import that the claim as a whole suggests for it.” *Bell Communications Research, Inc. v. Vitalink Communications Corp.*, 55 F.3d 615, 620, 34 USPQ2d 1816, 1820 (Fed. Cir. 1995). “If the claim preamble, when read in the context of the entire claim, recites limitations of the claim, or, if the claim preamble is ‘necessary to give life, meaning, and vitality’ to the claim, then the claim preamble should be construed as if in the balance of the claim.” *Pitney Bowes, Inc. v. Hewlett-Packard Co.*, 182 F.3d 1298, 1305, 51 USPQ2d 1161, 1165-66 (Fed. Cir. 1999). *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951) (A preamble reciting “An abrasive article” was deemed essential to point out the invention defined by claims to an article comprising abrasive grains and a hardened binder and the process of making it. The court stated “it is only by that phrase that it can be known that the subject matter defined by the claims is comprised as an abrasive article. Every union of substances capable *inter alia* of use as abrasive grains and a binder is not an ‘abrasive article.’” Therefore, the preamble served to further define the structure of the article produced.). In *Poly-America LP v. GSE Lining Tech. Inc.*, 383 F.3d 1303, 1310, 72 USPQ2d 1685, 1689 (Fed. Cir. 2004), the court stated that “a ‘[r]eview of the entirety of the ‘047 patent reveals that the preamble language relating to ‘blown-film’ does not state a purpose or an intended use of the invention, but rather discloses a fundamental characteristic of the claimed invention that is properly construed as a limitation of the claim . . . .” Additionally, clear reliance on the preamble during prosecution to distinguish the claimed invention from the prior art transforms the preamble into a claim limitation because such reliance indicates use of the preamble to define, in part, the claimed invention. See also MPEP § 2111.02.

Applicants submit that the term “for repeated, successive application within the same organism” in the preamble of claim 1 should be given patentable weight since the term gives “life, meaning, and vitality” to the claim and the term has been used to further define the claimed invention. Additionally, the term provides a fundamental characteristic of the claimed invention that is properly construed as a limitation of the claim analogous to the Federal Circuit’s holdings in *Kropa* and *Poly-America*. See also *In re Stencel*, 828 F.2d 751 (Fed. Cir. 1987) (holding that

the “purpose, set forth in the claims themselves, ‘is more than a mere statement of purpose; and that language is essential to particularly point out the invention defined by the claims.’”).

Furthermore, to support a *prima facie* conclusion of obviousness, the prior art must disclose or suggest all the limitations of the claimed invention. See *In re Lowry*, 32 F.3d 1579, 1582 (Fed. Cir. 1994).

Here, as the Examiner pointed out, the structure provided in Figure 25 of Dujon consists of a LTR sequence, a I-SceI recognition site, a selection marker, another copy of the LTR sequence, I-SceI recognition site and a second selection marker. Such a structure would not be suitable for the “repeated, successive application within the same organism” as required by the claim because, as explained in Figure 25B, the resulting construct would still contain one I-SceI recognition site, which prevents the repeated, successive application of the same recombination system in the same organism that is made possible only by flanking the recognition site or sites by homologous regions. Moreover, it is further noted that Figure 25B of Dujon provides only the possible modes of recombination that may occur intra-chromosomally. Accordingly, the construct shown in Figure 25B, part 1, illustrates only an intermediate that occurs during carrying out the method, but not a recombination system for repeated and successive application within the same organism. Accordingly, Dujon does not teach or suggest all the limitations of the claimed invention.

Additionally, it is well established that under 35 U.S.C. § 103 the Examiner must consider the reference as a whole, including portions that teach away from the claimed invention. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984). Additionally, if the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references normally do not render the claims obvious. *In re Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959) (The court reversed an obviousness rejection, stating that the “suggested combination of references would require a substantial reconstruction and redesign of the elements shown in [the primary reference] as well as a change in the basic principle under which the [primary reference] construction was designed to operate.” 270 F.2d at 813, 123 USPQ at 352.); see also MPEP § 2143.02 VI.

It is noted initially that, if the right I-SceI site of Dujon's construct were to be deleted as suggested by the Examiner, then the modes of recombination as proposed in parts 2) and 3) of Figure 25B would be inoperative. Upon recognizing such inoperability, one skilled artisan would not have been motivated to delete the right I-SceI site as suggested by the Examiner, since the construct would no longer function in the disclosed scheme. Furthermore, the only teaching in Dujon is either a vector having, in the 5' to 3' direction, a LTR sequence, a I-SceI recognition site, and a selection marker (a "LTR-I-SceI-selection marker unit"), or a vector comprising tandem repeats of such a LTR-I-SceI-selection marker unit. Dujon does not teach or suggest a vector comprising, in the 5' to 3' direction, a copy of the LTR-I-SceI-selection marker unit and an additional copy of a similar unit having the I-SceI site deleted. Thus, there are structural as well as use differences between the present claims and the prior art. To arrive to such a vector, one skilled in the art would have to rearrange the elements taught in Dujon to operate for a different purpose than is disclosed and which the reference does not suggest. Therefore, Dujon does not render the claims obvious within the meaning of 35 U.S.C. § 103. Reconsideration and withdrawal of the rejection is respectfully requested.

Separate consideration to the newly added claim 31 is respectfully requested. As discussed above, Dujon does not teach or suggest a recombination system using a construct containing at least two recognition sequences for site-directed induction of DNA double-strand break flanking by homologous regions. Furthermore, even if one skilled in the art would have been motivated to delete the right I-SceI site as allegedly by the Examiner, such a modification would not result in the system as claimed in claim 31. Accordingly, the Dujon reference does not render claim 31 obvious.

### **CONCLUSION**

For at least the above reasons, Applicants respectfully request withdrawal of the rejections and allowance of the claims. If any outstanding issues remain, the Examiner is invited to telephone the undersigned at the number given below.

This response is filed within the three-month period for response from the mailing of the Office Communication, to and including December 30, 2008. Applicants believe no fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 03-2775, under Order No. 13156-00216-US from which the undersigned is authorized to draw.

Respectfully submitted,

By /s/ Hui-Ju Wu

Hui-Ju Wu, Ph.D.

Registration No.: 57,209

CONNOLLY BOVE LODGE & HUTZ LLP

1007 North Orange Street

P. O. Box 2207

Wilmington, Delaware 19899-2207

(302) 658-9141

(302) 658-5614 (Fax)

Agent for Applicants

#640203